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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
LIU, SAMUEL W	
ART UNIT	**PAPER NUMBER**
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/723,247	BAR-OR, DAVID	
	Examiner	Art Unit	
	SAMUEL W. LIU	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 July 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *46,49-53,81,186,194-199,217-220,246,272,273 and 280-299* is/are pending in the application.

4a) Of the above claim(s) *none* is/are withdrawn from consideration.

5)☒ Claim(s) *272 and 273* is/are allowed.

6)☒ Claim(s) *46,49-52,81,186,194-199,217-220,246,280,282-286,289-293 and 295-299* is/are rejected.

7)☒ Claim(s) *53, 299, 281,287,288 and 294* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/15/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the claims

Claims 46, 49-53, 81, 186, 194-199, 217-220, 246, 272, 273 and 280-299 are pending.

The amendment filed 7/15/09 which amends claim 272 has been entered. Claims 1-45, 47-48, 54-80, 82-185, 187-193, 200-216, 221-245, 247-271 and 273-279 were cancelled by the amendment filed 11/20/06. Claims 46, 49-53, 81, 186, 194-199, 217-220, 246, 272-273 and 280-299 are examined in this Office action.

IDS

The references listed in IDS filed 7/15/09 have been considered by Examiner.

New-Claim Rejections - 35 USC §103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

[1] Claims 46, 49-52, 81, 186, 194-198, 217, 219, 220, 246, 280, 282-285, 289-292, 295, and 297-299 are rejected under 35 U.S.C. 103(a) as being unpatentable over Reynolds E. C. (US Pat. No. 6780844) in view of Jiang et al. (*J. Agric. Food Chem.* (2000) 48, 990-994) and Jacobson et al. (US 2002/0128298 A1).

Reynolds teaches a complex containing phosphopeptide stabilized amorphous calcium fluoride phosphate (col. 2, line 56 and 57, and col. 3, lines 8-11), and teach a pharmaceutical composition comprising said complex wherein the pharmaceutical

composition is a dental composition in a form of a gel, solid, powder or cream (col.7, lines 5-10) for treating dental caries or tooth decay (col. 3, lines 55-59), wherein the dental cream is toothpaste (col. 4, lines 27 and 28). Reynolds teaches that said the phosphopeptide is a casein protein fragment of SEQ ID NO:2, 3 or 4 wherein all SEQ ID NOs:2, 3 and 4 are partially phosphorylated (see patent claim 3) wherein one out of total five Ser residues (80%) are phosphorylated, i.e., 20% dephosphorylated.

Also, Reynolds teaches that the phosphopeptide stabilizes amorphous calcium phosphate (ACP), and teaches that the stabilized ACP is most soluble (col. 2, lines 14-17) wherein the stabilized and soluble ACP prevents caries and increases calcium bioavailability (col. 2, lines 17-20). These teachings are applied to claims 46, 50, 51, 186, 195-197, 219, 220, 246, 280, 282-284, 289-291, 297, 298 and 299.

The administration of dental composition toothpaste is a topical administration route (see [0040], lines 4-7, Jacobson et al.), as applied to claims 217 and 295.

Yet, Reynolds does not expressly teach that the phosphopeptide is phosvitin or fragment thereof nor teaches that the phosphopeptide is partially phosphorylated, e.g., 65% de-phosphorylated.

Jiang et al. teach that the partially phosphorylated (with 35% phosphates retention) phosvitin phosphopeptide ("PPP") inhibits calcium phosphate precipitation wherein 35% phosphate retention which is considered to be equivalent to about 65% de-phosphorylation thereof shows the highest capability of solubilization of the insoluble calcium phosphates (see Figure 5, p. 993, and p.994, left col., lines 10-12). Also, Jiang et al. teach that "PPP" is useful for a nutraceutical (p. 994, left column, last sentence) wherein the "nutraceutical" composition is a combination of nutrition and pharmaceutical

(see Wikipedia (2009, updated) "Nutraceutical", en.wikipedia.org/wiki/Nutraceutical, pages 1-8), and thus, the nutraceutical composition taught by Jiang et al. is considered o be a pharmaceutical composition. The Jiang et al. teachings are applied to claims 46, 50, 51, 186, 195-197, 280, 282-284 and 289-291.

Jiang et al. teach that PPP is obtained from hen egg yolk (page 991, left col., section "Materials"), as applied to claims 49 and 194.

Considering that "65%' read on "about 70%" wherein "about" renders "65%" applicable herein, claims 52, 198, 285 and 292 are included in the rejection.

Claim 81 is directed to a "kit" comprising instruction of using the kit, wherein said instruction is considered to have no patentable weight given by its own, and comprising a container holding the composition; wherein the "container" is obvious to any skilled artisan, and wherein the instruction and container will not alter the structure of the claimed pharmaceutical composition. See *In re Haller,* 73 USPQ 403 (CCPA 1946). Therefore, claim 81 is rejected.

It would have been obvious to one ordinary skill in the art at the time the invention was made to prepare the pharmaceutical composition such as in a gel or powder form of dental composition which comprises the dephosphorylated (~ 65%) phosvitin or fragment thereof. This is because of the reasons below.

Reynolds has taught that their phosphopeptide can be obtained from any source, such as phosphor-acid rich proteins, e.g., "phosphitin" (col. 2, lines 58-60); wherein the "phosphitin" is an alternative name of **phosvitin** (see "*Discussion of art*" [1] and [2]). Insoluble calcium phosphates limit their anticariogenic activity and have poor bioavailability (col. 2, lines 26-35, Reynolds), suggesting importance of solubilization of

the calcium phosphates. The phosphopeptides mediated fluoride-amorphous calcium phosphate phase localization at the tooth surface provides superior anticaries efficacy (col. 2, lines 43-48, Reynolds) due to the complex acting as a delivery vehicle that co-localizes calcium ions at a target site (col. 3, lines 48-52). The Reynolds' teachings are applied to claims 46, 49-51, 186, 194-197, 280, 282-284 and 289-191.

One of ordinary skill in the art would have substitute the phosvitin phosphopeptide for casein phosphopeptide and would have used the phosvitin phosphopeptide to form said complex in said pharmaceutical composition. This is because;

(**i**) Reynolds' phosphopeptide is partially phosphorylated, i.e., in the dephosphorylated (20%) state, and Jiang et al. also taught the dephosphorylated phosphopeptide (phosvitin fragment) useful as the pharmaceutical (see above discussion);

(**ii**) Reynolds has taught possibility of substitution of the casein phosphopeptide by the phosvitin phosphopeptide (col. 2, lines 58-60); and

(**iii**) Jiang et al. have taught that the phosvitin peptide with the 65% de-phosphorylated produces the highest degree of solubilization of calcium phosphate precipitation compared with the casein phosphopeptide (CPP) and the phosvitin phosphopeptide (PPP) having less than 65% dephosphorylation wherein the comparison shows that PPP is superior over CPP in solubilizing calcium (see above corresponding discussion), and have taught that phosphate content (i.e., dephosphorylation state) of the phosvitin phosphopeptide (PPP) has a critical effect on calcium binding ability thereby effect on said solubilization (see Fig,. 5, and page 993, right col., line 13 to page 994, left col. line 1).

In addition, Jiang et al. have compared phosvitin phosphopeptide (PPP) with casein phosphopeptide (CPP), and have shown that the PPP with 35% phosphate retention equivalent to the 65% dephosphorylated PPP is superior over said CPP (casein) with regard to inhibition of calcium phosphate precipitation, i.e., promoting satisfactory calcium solubilization (see Fig. 5 wherein "●" is CPP curve, and "■" is 65% dephosphorylated PPP curve). Jiang et al, explicitly teach that 35% phosphorylated (65% dephosphorylated) **phosvitin** can solubilize more calcium than CPP (**casein** phosphopeptide) (see page 994, left col., last 5 lines).

Since Reynolds' patent is directed to stable soluble calcium phosphate complex (col. 3, lines 14-18, and patent claim 1, line 1) mediated by the casein phosphopeptide, and since the phosvitin (CPP) is superior over casein (CPP) to inhibit precipitation thereby promote the solubilization of calcium thereof as taught by Jiang et al., and thereby increase calcium bioavailability for pharmaceutical application (see above), one of ordinary skill in the art would have chosen the phosvitin phosphopeptide (PPP) to produce the calcium phosphate complex.

Since the phosphorylation/dephosphorylation state of phosvitin peptide is critical for forming soluble (or preventing/inhibiting insoluble) calcium phosphate, and since it has been found that the 65% dephosphorylated phosvitin (PPP) is superior over casein (CPP) (see above), one of ordinary skill in the art would have TRIED to substitute the phosvitin phosphopeptide with 65% dephosphorylation for the casein phosphopeptide in the Reynolds' composition. When tried, it would have necessarily led to reasonable expectation of success. Therefore, combination of the references' teachings renders the claims *prima facie* obvious.

[2] Claims 186, 194, 218 and 296 are rejected under 35 U.S.C. 103(a) as being unpatentable over Reynolds E. C. (US Pat. No. 6780844 B1) in view of Jiang et al. (*J. Agric. Food Chem.* (2000) 48, 990-994) and Jacobson et al. (US 2002/0128298 A1) as applied to claims 186 and 194, and further in view of Shuch et al. (US Pat. No. 6503483).

The teachings of claims 186 and 194 by Reynolds, Jiang et al. and Jacobson et al. have been set forth above.

Yet, these three references do not expressly teach that the formulated composition is in drop form.

Shuch et al. teach that oral delivery system, i.e., formulation can be candy-gum "drops" (see col. 8, line 62 to col. 9, line 2), as applied to claim 218 and 296.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to formulate said composition as drops because "drops" refer to small quantity of the formulation of claims 218 or/and 296. In addition, choosing the "drops" formulation for delivery small quantity of the oral composition is well within purview of one of ordinary skill in the art dentistry when instant invention was made. The nexus between the "drops" form and the "dental composition" taught by Reynolds is that both Shuch et al. and Reynolds teach the dental composition, wherein the "drops" are suitable for topical application (col. 9, lines 4-5, Shuch et al.). Therefore, the references' teachings are *prima facie* obvious over instant claims in the absence of any unexpected result.

Conclusion

Claims 46, 49-52, 81, 186, 194-199, 217-220, 246, 280, 282-286, 289-293 and 295-299 are not allowed. Claims 53, 199, 281, 287, 288 and 294 are objected to as being dependent upon a rejected base claims 46 and 186, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. Claims 272-273 are allowed.

Discussion of the art

The prior art made of record and not currently relied upon in any rejections is considered pertinent to Applicants' disclosure:

(1) Ibanoglu et al. (*Food Chem.* (2007) 101, 626-636) teach two major egg yolk granule proteins **phosphitin** and high-density lipoprotein (HDL) by referring to Le Denmat et al. reference (page 628, right col., last paragraph).

(2) Le Denmat et al. (*Food Hydrocolloids* (2000) 14, 539-549) teach that hen egg yolk granule contains 70% HDL and 16% phosvitin; nowhere in this reference uses the term "phosphitin"; and thus, the "**phosphitin**" used in Ibanoglu et al. must be "**phosvitin**".

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Samuel Liu whose telephone number is (571)272-0949. The examiner can normally be reached on Monday-Friday, 9 am to 5:30 pro.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang, can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for

published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Samuel Wei Liu/
Patent Examiner, Art Unit 1656

/ANAND U DESAI/
Primary Examiner, Art Unit 1656

November 8, 2009